UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,298	07/02/2001	Steven M. Ruben	PZ035P1C1	4425

22195 7590 01/02/2003

HUMAN GENOME SCIENCES INC
9410 KEY WEST AVENUE
ROCKVILLE, MD 20850

EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/02/2003

7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/895,298	RUBEN ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) *1-10,13-15 and 17-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11, 12, 16 and 25-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-74* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-74 are pending in the instant application. Claims 25-74 have been added as requested by Applicant in Paper Number 5, filed Oct. 15, 2002.

Election/Restrictions

2. Applicant's election of Groups XLVIII-XCIV, drawn to polypeptides of SEQ ID NO: 83 and clone ID HPRBF19 in Paper No. 5 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-10, 13-15 and 17-24 are withdrawn as being drawn to a non-elected invention.

Claims 11, 12, 16 and 25-74 are currently under examination.

Information Disclosure Statement

3. The sequences disclosed in the IDS filed Oct. 15, 2002 (references AF-AS) have been considered to the extent that was possible absent an explanation of relevance or a sequence alignment.

Claim Objections

4.1 Claim 16 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

claim(s) in independent form. Claim 16 depends from claim 15, which is a non-elected invention.

4.2 Claims 30, 36, 38, 39, 43, 45, 46, 50, 52, 53, 57, 59, 60, 64, 69 and 74 are also objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. A method of producing a protein does not further limit the protein, and the recitation of an antibody that is capable of binding a protein in a Western blot or ELISA assay also does not further limit the protein.

4.3 Claim 11 is objected to as reciting an improper Markush Group. M.P.E.P. 803.02 states that:

> "Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

The limitations "SEQ ID NO:Y" and "ATCC Deposit No.Z" are each functionally equivalent to a Markush Group. The finite number of express and mutually exclusive embodiments encompassed by these limitations do not share a common utility which is based upon a shared structural feature lacking from the prior art.

Appropriate correction is required.

Priority

5. This application filed under former 37 CFR 1.60 lacks the current status of the nonprovisional parent application 09/591,316. A statement reading "(now abandoned)" should be included after "09/591,316, filed June 9, 2000" as the first sentence of the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6.1 Claims 11, 12, 16 and 25-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The protein of the instant invention is 33% identical to LAK-4p protein, which does not have a known specific activity, but is thought to be important in T-cell activation. The specification teaches that the protein of the instant invention can also activate the GAS (gamma activating sequence) promoter element, which is promoter element found upstream of many genes which are involved in the JAK-STAT pathway. The JAK-STAT signal transduction pathway is a large signal transduction pathway involved in the differentiation and proliferation of cells. The specification asserts that the gene encoding the polypeptide of SEQ ID NO: 83 can be used for differential identification of the tissues or cell types present in a biological sample for diagnosis of diseases and conditions which include, but are not limited to, cancer of the

reproductive systems. The specification states on page 66, lines 1-2, "This gene is expressed primarily in ovarian cancer, and to a lesser extent in breast cancer and prostate tissue." This is a specific and substantial utility. However, due to the brevity of the disclosure, it is not clear if the polypeptide could be used as an ovarian or breast cancer marker. Apart from the statement on page 66, there is no information on whether the protein is expressed in normal ovarian or breast tissue, if it is expressed differentially in prostate cancer compared to normal prostate tissue, or how many ovarian cancers or breast cancers express the polypeptide. In the paragraph bridging pages 66 and 67, the specification asserts that the tissue distribution and homology to LAK-4p indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of disorders of developing and growing systems, and cancers, and that the protein and antibodies directed against the protein may show utility as tumor markers and/or immunotherapy targets. However, due to the lack of guidance, the specification is not enabling for use of the polypeptide or polynucleotide for these uses. In order for a polypeptide or polynucleotide to be useful as a cancer marker, some basic expression data must be disclosed. For instance, the Guidelines for Marker Development by the National Cancer Institute (NCI) clearly indicate the data required to proceed, and the considerations for preliminary identification of a potentially useful marker in the initial step. Some of the considerations in the Guidelines are:

> "Step 1: ... Can a patient *population* be defined for which this marker may have utility? What is an expected range for the prevalence of this marker in population of potential interest? .... The number of specimens that should be assessed at this stage will vary depending on the question asked or the intended use of the marker. If *prevalence is being assessed,* then >20 specimens should be examined so that a marker present in 5% of cases would have a reasonable chance of being detected in the set of specimens. The numbers to be assessed for other questions will depend on the statistical design, the difference that would be meaningful to detect.

> .... Estimate prevalence of the marker on an *expanded* collection of targeted specimens.
> Step 5: ... The intended use should be more clearly defined and careful *statistical* designs applied to studies that usually have to include *large number of cases*."

None of the critical questions or considerations for the determination of a cancer marker above can be answered or met by the present application. Because no any data is disclosed in the specification as to the expression of the polypeptide in normal or cancer tissues, the specification has not provided the person of ordinary skill in the art the guidance necessary to be able to use the polypeptide as a cancer marker.

6.2 Claims 31-36, 44-50, 58-64 and 70-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 31-36, 44-50, 58-64 and 70-74 require the specific deposit recited in the claims to practice the invention. Applicants' referral to the deposit of cDNA clone HPRBF19 on page 129 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as

the Treaty leaves these specific matters to the discretion of each State. Additionally, amendment of the specification to recite the date of the deposit, the complete name and address of the depository, and the accession number of the deposited cell line is required.

6.3 Claims 11, 12, 16 and 37-74 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification describes a polypeptide sequence consisting of SEQ ID NO: 83, which has the activity of activating the GAS (gamma activating sequence) promoter element, and which may be useful as an ovarian or breast cancer marker. However, the claims as written include polypeptides comprising fragments and homologues, encompass polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of a single polypeptide, that of SEQ ID NO: 83 with the instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures,

diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 83. Protein function, however, cannot be reliably predicted from protein sequence homology. For example, Transforming Growth Factor (TGF-beta) Family OP-1 induces metanephrongenesis whereas closely related TGF-beta family members-BMP-2 and TGF-beta1-have no effect on metanephrogenesis under identical conditions (Vukicevic et al., 1996, PNAS USA 93:9021-9026). Platelet-derived Growth Factor (PDGF) Family VEGF, a member of the PDGF family, is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells while PDGF is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (Tischer et al., U.S. Patent 5,194,596, column 2, line 46 to column 3, line 2). Finally, vertebrate growth hormone of 198 amino acids becomes an antagonist (inhibitor of growth) when a single amino acid is changed (Kopchick et al, U.S. Patent No. 5,350,836). Even 99% homology does allow predictability in this instance. Given the unpredictability of

homology comparisons, and the fact that the specification fails to provide objective evidence that the additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. Further, even if the proposed consensus sequence were definitive of a genus with a specified function, the instantly claimed genus is not so limited and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polypeptides encompassed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 29, 35, 37-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7.1 Claims 37-64 are indefinite because claims 37, 44, 51 and 58 recite the limitation "specifically binds", it is not clear what this term means. The rejection would be withdrawn if the word "specifically" was deleted from the claims.

7.2 Claims 34, 62 and 72 are indefinite because they encompass a protein further comprising a polypeptide sequence heterologous to the HPRBF19 cDNA, and a polypeptide is always heterologous to a cDNA. It is recommended that the claims be amended to recite "to the polypeptide encoded by", as was done in claim 48.

7.3 Claims 29, 35, 42, 49, 56, 63, 68 and 73 are indefinite because they encompass a composition comprising a protein and an "acceptable" carrier, and it is not clear what the carrier is acceptable for.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 11 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Tiranti et al., GENE, Vol. 126, pages 269-278 (1993).

Claims 11 and 16 encompass an isolated polypeptide comprising an amino acid sequence at least 95% identical to a polypeptide epitope of SEQ ID NO: 83 and method of producing polypeptide.

Tiranti et al. disclose a protein identified as a mitochondrial single-stranded DNA-binding protein, which has 7 contiguous amino acids (amino acids 22-28) that are identical to amino acids 151-157 of SEQ ID NO: 83. Since the specification on page 153 identifies an epitope as containing a sequence of at least 4 amino acids, the protein of Tiranti et al. meets the limitation of the claims.

9. The art considered pertinent to the present application is Database GenEmbl:, Accession No. HUU91321, Jan. 10, 2000, which discloses a fragment of a chromosome which encodes amino acids 42-100 of SEQ ID NO: 83 (see attached sequence alignment). This reference does not teach or suggest what is being claimed, but is cited as a DNA encoding a large segment of the protein of the instant invention.

Conclusion

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600